

Claims 15, 31, 32, 34, 35, 38, and 40 have been amended, and new claims 47-49 have been added. Support for the amendments to the claims and for the new claims can be found in the claims and specification as originally filed. No new matter is believed to have been added.

Attached hereto is Appendix A, captioned "Version with Markings to Show Changes", which shows the amendments made to the title, specification, and claims using standard notation (underlining and bracketing). Appendix B presents the pending claims in rewritten form. Applicant respectfully requests reconsideration and allowance of the claims pending.

I. REJECTION UNDER 35 U.S.C. §101 and §112, First Paragraph

Claims 34-37 were rejected under 35 U.S.C. §101 and §112, first paragraph, on the basis that these claims allegedly lack patentable utility, and that one skilled in the art would therefore not know how to use the invention. While Applicant does not accede to the basis for the rejection, claim 37 has been canceled, rendering the rejection moot with respect to that claim. Applicant respectfully traverses this rejection with respect to claims 34-36.

The Office Action concedes at page 2, lines 16 through 22, that polypeptides comprising a disintegrin domain such as the polypeptides reflected by the claims of Sheppard *et al.* (U.S. Patent No. 6,265,199) have been determined to have patentable utility. The basis asserted in the Office Action for the rejection of claims 34-36 under 35 U.S.C. §101 and §112, first paragraph, appears to be that the polynucleotides of these claims do not encode a polypeptide having the activity of a disintegrin domain. However, the Examiner is requested to note that claims 34-36 all are expressly drawn to polynucleotides encoding polypeptides related to the disintegrin domain of SEQ ID NO:4 and *having disintegrin activity*. Therefore, the basis for the rejection does not appear to apply to the claims, and for at least these reasons Applicant respectfully requests that the rejection of claims 34-37 under 35 U.S.C. §101 and §112, first paragraph, be withdrawn.

II. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 34-37 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. While Applicant does not accede to the basis for the rejection, claim 37 has been canceled, rendering the rejection moot with respect to that claim. Applicant respectfully traverses this rejection with respect to claims 34-36.

The Office Action bases the rejection on the supposition that the claims relate to nucleic acids having "10% of nucleic acid sequence deviations ... in first codon positions" and encoding polypeptides differing at as many as 30% of the positions in the amino acid sequence of SEQ ID NO:4 (see the top of page 5 of the Office Action). However, this calculation is completely inapposite to the claims, as claims 34 and 35 recite "at least 80 percent *amino acid* identity" and "at least 90 percent *amino acid* identity" (emphasis added), respectively. Therefore, the polypeptides encoded by the nucleic acid molecules of claims 34 and 35 could vary from amino acids 496 through 599 of SEQ ID NO:4 by at most 20% (claim 34) or 10% (claim 35), and do *not* differ from SEQ ID NO:4 by the 30% asserted by the Office Action as the basis for the rejection.

Furthermore, the description of the invention is to be assessed from the viewpoint of one of skill in the art. The Office Action incorrectly states "... skilled artisans in the relevant field of molecular biology could not predict the structure, or other properties, of the claimed products" (Office Action, bottom of page 5). As shown *inter alia* by Exhibit 1 previously submitted with Applicant's Response to Office Action of August 2002 (Jia *et al.*, 1997, *J. Biol. Chem.* 272: 13094-13102) and references cited therein, those of skill in the art would be aware of research elucidating the three-dimensional structure of disintegrin domains, and of the effect of changes in amino acid sequence on the disintegrin activity of these domains. Given the knowledge of the skilled artisan regarding these structure/function relationships for disintegrin domains, Applicant's disclosure is sufficient to describe to the skilled artisan the invention as claimed in claims 34-36.

For at least the above reasons, withdrawal of the rejection of claims 34-37 is respectfully requested.

Claims 34-37 were also rejected under 35 U.S.C. §112, first paragraph because the specification, while being enabling for preparation of nucleic acid sequences encoding fragments of SEQ ID NO:4 having disintegrin activity and such an encoded fragment of SEQ ID NO:4, allegedly does not reasonably provide enablement for preparation of nucleic acid sequence encoding a polypeptide having an amino acid sequence that diverges, by virtue of amino acid substitutions, deletions and insertions, or combinations thereof at as many as 30% of the amino acid positions from that of SEQ ID NO:4. While Applicant does not accede to the basis for the rejection, claim 37 has been canceled, rendering the rejection moot with respect to that claim. Applicant respectfully traverses this rejection with respect to claims 34-36.

For the reasons stated in the preceding paragraphs, claims 34 and 35 are *not* drawn to polynucleotides encoding polypeptides differing at as many as 30% of amino acid positions from SEQ ID NO:4. The Office Action states in support of the rejection that "no other metalloprotease-disintegrin of the class represented by the amino acid sequence of SEQ ID NO:4 has had as many as 250 amino acids specifically identified for concurrent modification" (the Office Action, page 7, lines 18-20); however this statement is completely inapposite to claims 34 and 35 as presented. Claims 34 and 35 are drawn to nucleic acid molecules encoding polypeptides sharing at least 80 or 90 percent amino acid identity, respectively, to amino acids 496 through 599 of SEQ ID NO:4; therefore the polypeptide variants of these claims would differ by, at most, 20 or 10 amino acids, respectively, when compared to amino acids 496 through 599 of SEQ ID NO:4. Therefore, the hypothetical situation proposed by the Office Action in support of its assertion of non-enablement of the claims — differing by "as many as 250 amino acids" — is not at all apposite to claims 34-36 as presented.

For at least the foregoing reasons, Applicant respectfully requests withdrawal of the rejection of claims 34-37 under 35 U.S.C. §112, first paragraph.

III. REJECTION UNDER 35 U.S.C. §102(a) and 35 U.S.C. §102(e)

Claims 15, 31, 38, and 39 were rejected under 35 U.S.C. §102(a) as allegedly being anticipated by Hillier *et al.* (GenBank Accession No. R15308). Although Applicant does not accede to the basis for the rejection, claim 39 has been canceled, rendering the rejection moot with respect to claim 39, and claims 15, 31, and 38 have been amended. The disclosure of Hillier *et al.* is not relevant to claims 15, 31, and 38 as presented; withdrawal of the rejection of claims 15, 31, 38, and 39 under 35 U.S.C. §102(a) is respectfully requested.

Claims 15, 16, 21-23, 30-32, 34-40, 42, and 44-46 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 6,265,199 to Sheppard *et al.* Applicant does not accede to the basis for the rejection and traverses the rejection under §102(e) for the following reasons. The Sheppard *et al.* '199 patent cannot be entitled to a 102(e) date earlier than July 10, 1998, which is the filing date of the provisional application to which the Sheppard *et al.* '199 patent claims priority under §119(e). However, the present application of Applicant claims the benefit of a priority application filed on February 11, 1998. Therefore, the Sheppard *et al.* '199 patent cannot be prior art under §102(e) to claims 15, 16, 21-23, 30-32, 34-40, 42, and 44-46, which are supported by the disclosure of Applicant's February 11, 1998 priority application.

For at least the above reasons, Applicant respectfully requests withdrawal of the rejection of claims 15, 16, 21-23, 30-32, 34-40, 42, and 44-46 under 35 U.S.C. §102(e).

IV. OBJECTIONS TO THE CLAIMS

The Applicant gratefully acknowledges the Office Action's statement (at page 9, lines 4-6 of the Office Action) that claims 33, 41, and 43 would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims. Claims 33, 41, and 43 have been so rewritten and are presented as new independent claims 47-49; the dependent claims 33, 41, and 43 have been canceled.

Should the Examiner have any questions, or believes that a teleconference would be helpful to clarify prosecution or to advance the present application to allowance, the Examiner is invited to call the undersigned attorney at (206) 265-4071.

The Examiner is authorized to charge any required fees or credit any overpayments to Deposit Account Number 09-0089.

Respectfully submitted,



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